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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/506,734	10/31/2005	Timothy S. Gardner	0079571-0141	7041

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EXAMINER	
RIGGS II, LARRY D	

ART UNIT	PAPER NUMBER
1631	

NOTIFICATION DATE	DELIVERY MODE
12/09/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentdocket@choate.com

Office Action Summary	Application No.	Applicant(s)	
	10/506,734	GARDNER ET AL.	
	Examiner	Art Unit	
	LARRY D. RIGGS II	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-85* is/are pending in the application.

4a) Of the above claim(s) *1-58,66-76,78-83 and 85* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *59-65,77 and 84* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *22 June 2006, 06 October 2006 and 17 August 2009*
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of Group III, claims 59-65, 77 and 84 in the reply filed on 24 July 2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-58, 66-76, 78-83 and 85 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 24 July 2009.

Status of Claims

Claims 1-85 are currently pending. Claims 1-58, 66-76, 78-83 and 85 are withdrawn. Claims 59-65, 77 and 84 are examined on the merits.

Information Disclosure Statement

The information disclosure statements filed 22 June 2006, 06 October 2006 and 17 August 2009 are acknowledged. Signed copies of the corresponding 1449 forms have been included with this Office action.

Drawings

The amended drawings filed on 03 September 2004 are accepted.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, (see specification, paragraphs 87, 115, 253, 301 and 307). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 59-65, 77 and 84 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 59 recites the limitation “determining the response of at least one of the biochemical species in the biological network to the compound" in lines 8-9. There is insufficient antecedent basis for the response...to “the compound" because there was no exposing of species of the network to "a compound”. It is noted that line 6 of claim 59 recites perturbing a species IN the network, but does not limit the perturbation to comprise a compound.

Claims 59 recites the limitation “calculating predicted perturbations of biochemical species in the biological network that would be expected to yield the determined responses according to the model” in lines 10-12. It is unclear to what the

limitation “would be expected to yield the determined responses according to the model” pertains. The model of claim 1 provides parameter estimates. Previously in claim 59, there is only one response of species to the compound, there are no "responses”. It is unclear what “would be expected” in the “determined responses”. It is unclear if the “determined responses” are from a species exposed to different compounds, multiple species exposed to one compound, species exposed to different experimental parameters or different genetic mutations. Likewise, it is unclear if the “predicted perturbations” are exposing the species of the network only to “the compound”, compounds, any chemical, agent, genetic mutation, or experimental parameters.

Claims 77 and 84 recite the limitation “calculating predicted perturbations of biochemical species in the biological network that would be expected to yield the determined responses according to the model”. It is unclear to what the limitation “would be expected to yield the determined responses according to the model” pertains. Step (ii) provides data comprising responses of species to “the perturbation”, but it is unclear if the calculated “predicted perturbations” are expected to yield the “responses” of step (ii) or different “responses” than the "responses" of step (ii), because the calculated "predicted perturbations" encompass more than one perturbation and it is unclear if these “predicted perturbations” are the same as the single “perturbation” of step (ii).

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 59-65 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The recent en banc decision regarding Bilski v. Warsaw (2008) set forth that a process is patent-eligible if (1) it is ties to a particular machine or apparatus or (2) it transforms a particular article into a different state or thing.

The instant claims are drawn to a method of identifying a target of a perturbation. The instant claims are drawn to the abstract process steps of providing a biological system comprising a network of a plurality of species, providing or generating a model of the biological system, perturbing the species in the network, allowing the network reach a steady state, determine the response of the species, and calculate predicted perturbations of the species that would be expected to yield the determined response according to the model. The instant claims do not recite or inherently involve any transformation of an article, nor do they recite any limitation that ties one or more specific steps of the process to any particular machine or apparatus.

Nominal or token recitations will not suffice, E.g. displaying, inputting, obtaining, See Ex parte Langemyr (May 28, 2008). Applicants are cautioned against introduction of new matter in an amendment.

For these reasons, claims 59-65 are considered non-statutory subject matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 59-63, 77 and 84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stoughton et al. (US 6,132,969) (IDS filed 10/6/06) in view of Lew et al. (J. Clin. Invest., 1991, 87, 100-112).

The instant claims are drawn to a method of identifying a target of a perturbation comprising the steps of providing a biological system comprising a network of a plurality of species, providing or generating a model of the biological system, perturbing the species in the network, allowing the network reach a steady state, determining the response of the species, and calculating predicted perturbations of the species that would be expected to yield the determined response according to the model.

In light of the indefiniteness of the instant claims shown above, the limitation “calculate predicted perturbations of the species that would be expected to yield the determined response according to the model" is interpreted as calculating the perturbations that would provide a desired response in a network of species based on a model of that network of species.

Regarding claims 59, 77 and 84, Stoughton et al. shows a biological network of cellular constituents, network models, quantitative measures suitable for expressing changes observed in the cellular constituents during experiments on a biological system, predictions of changes in cellular constituents according to a network model and assessment of the goodness of fit of a prediction to experimental results as suitably expressed, (column 6, last paragraph – column 7, first paragraph; Figure 1). Stoughton et al. shows a perturbation in the form of a compound (drug), (column 7, last paragraph; column 43, lines 30-62). Stoughton et al. shows computer systems, including memory with software and processors, for carrying out the computational steps of the method, (abstract; column 54-56; Figures 12 and 13).

Stoughton et al. does not show allowing the biological network to reach a steady state.

Lew et al. shows a mathematical model of volume, pH and ion current regulation in reticulocytes, (abstract). Lew et al. shows a model of a pH dependence of the K:Cl cotransport and Na pathways, that result in new steady state from the original reference state following transient perturbations, (page 103, right column, last paragraph – page 105, left column, first full paragraph; Figures 1, 2, 5, 6 and 9).

Regarding claim 60, Stoughton et al. shows targeting a protein with a drug known to interact with the targeted protein, (43, lines 30-62).

Regarding claims 61-63, Stoughton et al. shows statistical tests of the significance of the goodness of the overall fit found for the network model, (column 10, lines 31-40; column 23, line 37 – column 26, line 50). Stoughton et al. shows a cellular constituent can be assigned to the greatest output class where a threshold can be set for the sum of constituents, (column 22- line 52 – column 23, line 20).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of testing biological network models of Stoughton et al. by allowing the biological network reach a steady state after perturbation as in Lew et al. because Lew et al. shows that a steady-state different from the original steady-state may result from perturbations of a network, (page 103, right column, last paragraph – page 104, left column, first paragraph).

Claims 59-64, 77 and 84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stoughton et al. (US 6,132,969) in view of Lew et al. (J. Clin. Invest., 1991, 87, 100-112) as applied to claims 59-63, 77 and 84 above, and further in view of Wannenburg et al., (Am. J. Physiol. Heart Cir. Physiol., 2000, 279, H779-H790).

The instant claim 64 depends from claim 59 with the extra limitation wherein a predicted perturbation is identified as statically significant using a statistical test from the group consisting of z-test, t-test and chi-squared test.

Stoughton et al. and Lew et al. are applied to claims 59-63, 77 and 84 above.

Stoughton et al. and Lew et al. do not show a statistical test from the group consisting of z-test, t-test and chi-squared test.

Wannenburg et al. shows the effect of calcium activation on characteristic frequency parameters using statistical tests, in individual rat cardiac trabeculae, (abstract; page H785, left column, second paragraph; Figure 4; Table 2).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of testing biological network models of Stoughton et al. and Lew et al. with the confirmation of a significant perturbation via a statistical test by Wannenburg et al. because Wannenburg et al. shows that statistical test, e.g. t-test help determine which parameter in a system may be significantly perturbed with respect to other parameters in that system, e.g. b and c characteristic frequencies, (page H785, left column, second paragraph; Figure 4; Table 2).

Claims 59-63, 65, 77 and 84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stoughton et al. (US 6,132,969) in view of Lew et al. (J. Clin. Invest., 1991, 87, 100-112) as applied to claims 59-63, 77 and 84 above, and further in view of Scheidt et al., (J. Neurophysiol. 2001, 86, 971-985).

The instant claim 65 depends from claim 59 with the extra limitation the statistical test is used with estimates of moments of the probability density functions of the predicted perturbations.

Stoughton et al. and Lew et al. are applied to claims 59-63, 77 and 84 above.

Stoughton et al. and Lew et al. do not show the statistical test is used with estimates of moments of the probability density functions of the predicted perturbations.

Scheidt et al. shows Gaussian and bimodal probability density functions of perturbation sequence trials, (Figure 2), wherein a t-test determined that the unimodal and bimodal experiments were not significantly different, (page 981, right column, last paragraph).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of testing biological network models of Stoughton et al. and Lew et al. with the probability density function and a statistical test by Scheidt et al. because Scheidt et al. shows that probability density function distribution of moments combined with a statistical test, e.g. t-test, help determine whether a probability density is significant (page 981, right column, last paragraph), and one skilled in the art would recognize that moments of probability distribution function about responses of biochemical species and response of values of perturbations would better

determine the significance of a perturbation of a particular biochemical species when assessed by a statistical test, e.g. t-test.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LARRY D. RIGGS II whose telephone number is (571)270-3062. The examiner can normally be reached on Monday-Thursday, 7:30AM-5:00PM, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/LDR/
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